**Remarks**

Claims 3-10, 12-20, 24-27 are pending.

Claims 1, 2, and 11 have been canceled. Claims 3, 8-10, 12, 13, 17, 18, 20, and 24 have been amended. New claims 25-27 have been added..

Claims previously dependent on claim 1 have been rendered dependent on claim 24.

Claims 10, 17, 18, and 20 have been amended by replacing the term "ligand" with the term "antibody molecule."

Independent claim 24 has been modified by replacing the term "lipid-comprising vesicle" with the term "liposome." Furthermore, in claim 24 the expression "said antibody molecule being capable of binding to a HLA-DR" has been replaced with the expression "said formulation binding to a HLA-DR". The wording of claim 24 has also been rearranged for purpose of clarity.

The Applicant has also introduced new claims 25 to 27. Support for new claim 26 may be found in claims 2 and 24 as well as specification page 19, first line. Support for new claims 25 and 27 may be found in the specification at page 5, line 16.

No new matter has been added with the amendments or the addition of the new claims, which are intended to merely clarify language used in the claims and the subject matter claimed. The scope of the claims is intended to be the same after the amendment as it was before the amendment.

**Rejection based under 35 U.S.C. § 112, first paragraph**

The Examiner rejected claims 1-10 and 17-20 on the grounds that the specification is not enabling and/or does not provide a written description of the claimed formulation.

As indicated above, independent claim 1 and claim 2 have been canceled and the dependency of the claims has been changed to be now dependent on claim 24. Therefore the Applicant respectfully submits that the Examiner's objection of claims 1-10 and 17-20 be withdrawn.

To the Examiner's own admission, results obtained for liposomes conjugated with an anti-CD4 antibody support the non-predictability of targeting liposome to all infectious agents and all cell types (Phillips *et al.*). Since, to the Examiner's opinion, the teaching of such formulation are not reliable, the Applicant respectfully submits that rejection of the present

claims in light of Selvam *et al.* and Desormeaux *et al.*, which both discuss similar formulations be withdrawn.

Nevertheless, the Applicant respectfully submits that the Examiner's discussion of the usefulness (i.e., related to an apparently reduced *in vivo* activity) of Phillips' formulation is irrelevant to the capacity of Phillips' formulation to target cells expressing CD4. For example, at the bridging paragraph of pages 3170-3171, Phillips *et al.* clearly indicate that the reduced *in vivo* efficacy of their formulation was not due to its lack of interaction with cells expressing CD4;

> "*PBMC isolated from mice treated with GK1.5 IgG immunoliposomes or GK1.5F(ab)2 immunoliposomes were able to interact with phycoerythrin-labeled monoclonal rat anti-mouse CD4 in vitro to the same extent*"

It is submitted that the present claims satisfy the requirements of Section 112(1) and are fully enabled by the specification. Accordingly, withdrawal of the rejections of the claims under Section 112 is respectfully requested.

**Rejection based under 35 U.S.C. 102 (b)**

The Examiner rejected claims 1-2, 10-20, and 24 under 35 U.S.C. § 102(b) as anticipated by EP 0286418A1 as evidenced by Sarloos *et al.* This rejection is respectfully traversed.

As indicated above, claims 1 and 2 have been canceled, and claim 24 has been amended.

The Applicant respectfully submits that EP 0286418A1 does not teach or suggest a formulation comprising an antibody molecule coupled to a liposome, where the formulation binds to a HLA-DR protein present at the surface of an infectious agent and at the membrane surface of a cell as claimed in amended claim 24.

In fact, liposomal formulations comprising "*antibody or antibody fragments (directed) either against CD4 or against coat polyprotein of the (HIV) virus*", as discussed in EP 0286418A1 (page 15, lines 20-30) do not anticipate a formulation that binds to both HLA-DR protein present at the surface of an infectious agent and at the membrane surface of a cell.

Neither does, liposomal formulation "useful to target the CD4 and ClassII antigens (as part of HIV binding site), gp120 (viral outer coat protein), gp41 (viral inner coat protein) and

other antigenic determinants characteristic of either the virus or the host cell", anticipate a formulation that binds to both HLA-DR protein present at the surface of an infectious agent and at the membrane surface of a cell.

In fact, EP 0286418A1 only refers to the use of liposome for interaction with "particular cell types" and not to "a formulation that binds to both HLA-DR protein present at the surface of an infectious agent and at the membrane surface of a cell."

In light of the foregoing amendments and arguments, withdrawal of the rejection of claim 24 and claims dependent therefrom is respectfully requested.

**Rejection based under 35 U.S.C. § 103 (a)**

Rejection of claims 3-9 and 19

The Examiner rejected claims 1-2, 10-18 and 24 under 35 U.S.C. 103(a) as being unpatentable over Selvam *et al.* or Desormeaux *et al.* in view of Sarloos *et al.* and Cantin *et al.* This rejection is respectfully traversed.

As indicated above, claims 1, 2, and 11 have been canceled and claim 24 has been amended. In view of the Examiner's position as to the non-reliability of Phillips *et al.* discussing liposome formulations comprising anti-CD4 antibody, the Applicant respectfully submits that the objections related to the Selvam *et al.* and Desormeaux *et al.* references be withdrawn.

Nevertheless, the Applicant respectfully submits that to the contrary of the Examiner's assertions, Selvam *et al.* does not teach an anti-CD4 molecule able to bind to CD4 expressed on infectious agent such as HIV.

As the Examiner points out, Selvam *et al.* clearly states at page 12, first column, last paragraph that;

> "*We tagged the liposomes with anti-CD4 monoclonal antibody, which allows them to be targeted to specific cell population...*"

and later;

> "*We demonstrate here the use of antibody-targeted liposomes for the intracellular delivery of phosphorothioate antisense complementary to HIV rev region.*"

The Applicant respectfully submits that there is no teaching or suggestion in Selvam *et al.* of an antibody molecule binding to a protein present at the surface of an infectious agent, and even less of a formulation which binds to a HLA-DR present at the surface of an infectious agent. Therefore, the Applicant respectfully submits that Selvam *et al.* does not teach or suggest a formulation which binds to both HLA-DR protein present at the surface of an infectious agent and at the membrane surface of a cell as claimed in independent claims 24 and dependent claims therefrom.

Additionally, to the Examiner's opinion, Saarloos et al. teach "a ligand such as an anti-HLA-DR that binds to HLA-DR protein present at the surface of an infectious agent such as HIV and at the membrane surface of a cell such as CD4+ T cells and macrophage". To the contrary of the Examiner's assertions, the Applicant was not able to locate any passage in Saarloos et al., which discussed a ligand binding to HLA-DR present at the membrane surface of a cell such as CD4+ T cells and macrophage.

The Applicant respectfully submits that nowhere does Saarloos et al. discuss such a ligand. The Applicant respectfully requests the Examiner to identify such passage within Saarloos in support of the Examiner's assertion.

In addition, neither Saarloos *et al.* nor Cantin *et al.* cure the deficiencies of Selvam *et al.* There is no motivation to combine the cited references as none of them teach or suggest a formulation (comprising a liposome and antibody molecule), which binds to a protein present at the surface of an infectious agent.

In light of the foregoing, withdrawal of the rejection of claim 24 and claims dependent therefrom is respectfully requested.

The Applicant further respectfully submits that there is no teaching or suggestion in Desormeaux *et al.* of an antibody molecule binding to a HLA-DR present at the surface of an infectious agent. Therefore, the Applicant respectfully submits that Desormeaux *et al.* does not teach or suggest a formulation that binds to both HLA-DR protein present at the surface of an infectious agent and at the membrane surface of a cell as claimed in independent claim 24.

Neither Saarloos *et al.* nor Cantin *et al.* cures the deficiencies of Desormeaux *et al.* There is no motivation to combine the cited references as none of them teaches or suggests a

formulation (comprising a liposome and antibody molecule) which binds to a protein present at the surface of an infectious agent and at the membrane surface of a cell as claimed in independent claims 24 and 25. As such, one of ordinary skill in the art would not have been led to the claimed invention.

Furthermore, no motivation to combine the teachings of Desormeaux *et al.*, either with those of Cantin *et al.* or with those of Saarloos *et al.*, can be found in the cited references. For example, although Desormeaux *et al.* is a review article specifically discussing the field of "Liposomes as Drug Delivery System: A Strategic approach for the Treatment of HIV Infection" there is no reference to the teachings of neither Cantin *et al.* nor Saarloos *et al.*, even though they were both available to the public at the time Desormeaux *et al.*, was submitted.

In light of the foregoing, withdrawal of the rejection of claim 24 and claims dependent therefrom is respectfully requested.

The Examiner's position is that the present invention is made obvious by simply substituting the anti-CD4 antibody of Selvam *et al.* or Desormeaux *et al.* for the anti-HLA-DR antibody of Saarloos *et al.* However, again the Applicant respectfully submits that there is no teachings, evidence or suggestion, in Selvam *et al.*, Desormeaux *et al.*, Saarloos *et al.* and/or Cantin *et al.*, either taken alone or in combination, of a formulation (comprising a liposome and antibody molecule) that binds to a HLA-DR protein present at the surface of an infectious agent.

As such, neither Selvam *et al.*, Desormeaux *et al.*, Saarloos *et al.* and/or Cantin *et al.*, taken alone or in combination, teach nor suggest a formulation which binds to both HLA-DR protein present at the surface of an infectious agent and at the membrane surface of a cell as claimed in independent claims 24 and 25 and dependent claims therefrom. Therefore, one of ordinary skill in the art would not have been led to the claimed invention.

The Examiner's position is that "as long as cells expressing HLA-DR or any infectious agent expressing HLA-DR, the anti-HLA-DR antibody taught by Saarloos et al. being coupled to any liposome taught by Selvam et al. or Desormeaux et al. would have targeted the liposome to said cell or said infectious agent such as HIV expressing HLA-DR". The Applicant respectfully submits that there is no basis in the cited reference for such assertion by the Examiner. Again, the Applicant reiterates that none of the cited reference teaches or suggests a formulation that that binds to both HLA-DR protein present at the surface of an infectious agent and at the

membrane surface of a cell and even more particularly to HLA-DR protein present at the surface of an infectious agent.

Again, the Applicant respectfully submits that the population of cells expressing HLA-DR is not necessarily the same population as those expressing CD4. Similarly, the population of virus carrying HLA-DR is not necessarily the same population as those carrying CD4. This fact has been exemplified in Saarloos *et al.*, for example at page 1642, first and second columns:

*"It was somewhat unexpected, then to find that HLA-DR was not detected on all the plasma virus samples tested"*

and

*"Thus, the variation in levels of HLA-DR expression on plasma virus may be due to the plasma virus budding from more than one cell type or, alternatively, from several subpopulations of one cell type."*

The Applicant further points out that the infectious agent is not any infectious agent — but one that bears HLA-DR at its surface. Similarly, the cell is not any cell —but a cell that possesses HLA-DR at its membrane surface. Amended claim 24 clearly specifies the above.

Considering the burden of HIV infection throughout the world there is a need to target both the virus and cells using every therapeutic approach possible, including targeting cells and infectious agents carrying HLA-DR.

In light of the foregoing, withdrawal of the rejection of the claim 24 and claims dependent therefrom is respectfully requested.

Rejection of claims 3-9 and 19

The Examiner rejected claims 3-9 and 19 under 35 U.S.C. § 103(a) as unpatentable over Selvam *et al.* or Desormeaux *et al.*, each in view of Saarloos *et al.* and Cantin *et al.*, and further in view of US Pat. No. 5,773,027 ('027). This rejection is respectfully traversed.

The teachings of Selvam *et al.*, Desormeaux *et al.*, Saarloos *et al.*, and Cantin *et al.*, have been discussed above. The Applicant respectfully submits that the teachings of the '027 patent do not cure the deficiencies of the cited references.

The added disclosure of the '027 patent with the above mentioned cited references does not teach nor suggest a formulation which binds to both HLA-DR protein present at the surface of an infectious agent and at the membrane surface of a cell — and even less such a formulation having the composition as claimed in claims 3-9, or further comprising a drug as claimed in claim 19. Therefore, using the teachings of the cited references, one of ordinary skill in the art would not have been led to the claimed invention.

In light of the foregoing, withdrawal of the rejection of claims 3-9 and 19 is respectfully requested.

Rejection of claims 11 and 20

The Examiner rejected claims 11 and 20 under 35 U.S.C. § 103(a) as unpatentable over Selvam *et al.* or Desormeaux *et al.*, each in view of Saarloos *et al.*, and Cantin *et al.*, and further in view of Harlow *et al.* This rejection is respectfully traversed.

As indicated herein, claim 11 has been canceled.

The teachings of Selvam *et al.*, Desormeaux *et al.*, Saarloos *et al.*, and Cantin *et al.*, have been discussed above. The Applicant respectfully submits that the teachings of Harlow et *al.* do not cure the deficiencies of the cited references.

The added disclosure of Harlow et *al.* with the above mentioned cited references does not teach nor suggest a formulation which binds to both HLA-DR protein present at the surface of an infectious agent and at the membrane surface and even less a formulation wherein the antibody molecule is an anti-Fab' antibody fragment as claimed in claim 20. Therefore, using the teachings of the cited references, one of ordinary skill in the art would not have been led to the claimed invention.

In light of the foregoing, withdrawal of the rejection of claim 20 is respectfully requested.

Rejection of claims 1-9

The Examiner rejected claims 1-9 under 35 U.S.C. § 103(a) as unpatentable over EP 0286418 A1, in view of Saarloos *et al.* and US Pat. No. 5,773,027 ('027). This rejection is respectfully traversed.

As indicated herein, claims 1 and 2 have been canceled.

The teachings of EP 0286418 A1 and Saarloos *et al.* have been discussed above. The Applicant respectfully submits that the teachings of the '027 patent do not cure the deficiencies of the cited references.

The added disclosure of the'027 patent with the above mentioned cited references does not teach nor suggest a formulation which binds to both HLA-DR protein present at the surface of an infectious agent and at the membrane surface of a cell and even less such formulation having the composition defined in claims 3-9. Therefore, using the teachings of the cited references, one of ordinary skill in the art would not have been led to the claimed invention.

In light of the foregoing, withdrawal of the rejection of claims 3-9 is respectfully requested.

**Extension of Term.** The proceedings herein are for a patent application and the provisions of 37 CFR § 1.136 apply. Applicant believes that a one-month extension of term is required. Please charge the required fee (large entity) to Account No. 23-2053. If an additional extension is required, please consider this a petition therefor, and charge the required fee to Account No. 23-2053.

Based on the above remarks, the Examiner is respectfully requested to reconsider and withdraw the rejections of the claims. It is submitted that the present claims are in condition for allowance, and notification to that effect is respectfully requested.

Respectfully submitted,

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